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Annual Report on the Medical Research Institute for the year 1923.

BLACKWATER FEVER.

Blackwater fever, or Hæmoglobinuric fever has been the subject of much controversy with regard to its causation. As experience has grown and careful observations and records have accumulated, the balance of evidence has swung more and more definitely to the malarial origin of the disease. Nevertheless, from time to time, new theories arise and other parasites are described as of pathogenic importance.

Blackwater fever has one sign common to all cases, that is the passing of urine which is coloured some shade of red or brown according to the amount of blood-colouring matter it contains and dependent on the time at which the urine is voided after having reached the bladder. But the sequence of events, the nature of the onset, the number and the severity of the general signs and symptoms, the course of the disease, all these vary within fairly wide limits in different cases, in West Africa, at any rate. That these are dependent on individual idiosyncrasy and are influenced by the amount and degree of previous malarial infection, attacks, moreover, for the most part inefficiently treated, is probably the correct view, but this very lack of uniformity has led many observers to seek for other explanations.

One of the most recent papers on the subject, contributed by Dr. Lefrou and Dr. Blanchard, describes the finding of spirochætes in the blood of several cases of blackwater fever, which occurred in French Congo. These observers, by using the method of triple centrifugation of the blood, isolated *Leptospira* from the third deposit, which they were successful in transferring to guinea-pigs.

During the year under review, an opportunity was afforded at Yaba of examining four cases of the disease by this method. Three of these occurred in Lagos (one was probably a simple hæmoglobinuria) and one in Abeokuta. The technique consists in withdrawing a certain quantity of the patient's blood from a vein, into a measured amount of a solution of Citrate of Sodium of a definite strength, in a tube.

The mixture is then centrifugalised, the rate and the time being controlled. The first sediment which consists mainly of red and white cells is discarded.

The supernatant fluid is again centrifugalised during which the remainder of the red cells and most of the blood-platelets are brought down. The second deposit is also thrown away, and the fluid is centrifugalised a third time. The deposit, on this occasion contains some blood-platelets and any spirochætes which may be present.

In all the four cases investigated by this method, structures were readily found which by the dark-ground illumination of wet films closely resembled spirochætes. The deposit in each case was submitted to other tests, smears were fixed and stained by Giemsa's process and also by Fontana's preparation, cultures were made and guinea-pigs were inoculated. The staining methods failed to reveal spirochætes, the attempts at cultivation in artificial media were negative, and although spirochæte-like structures were seen in the blood of the inoculated guinea-pigs, the animals themselves, with one exception showed no ill-effects. In the first case of blackwater fever five series of sub-inoculations were carried out from guinea-pig to guinea-pig, a similar number in the second and third cases, and four series in the last case. In the second case, one guinea-pig in the third series of sub-inoculations, showed a blood-serum stained distinctly pink after centrifugalisation. This however, was almost certainly due to artificial laking. The failure to demonstrate spirochætes except by dark-ground illumination directed attention to the examination of the blood, in health and in disease both in human beings and in laboratory animals.

About this time word was received that Dr. J. G. Thomson of the School of Tropical Medicine, London, was investigating the condition in Rhodesia and held the belief that the structures described were "pseudo-spirochaetes" and unconnected with the illness. The blood of five Europeans was examined, two of whom had suffered from black-water fever in the past, one who was recovering from amoebic dysentery, and two who were convalescent from sub-tertian malaria. A native who harboured *Filaria loa* was also included. In addition to these, the blood of six monkeys and eight guinea-pigs was also examined. The "pseudo-spirochaetes" were readily found in all cases. The slowness of their movements, the small number and irregularity of their spirals and the fact that they are not highly refractile draw attention to their non-parasitic nature. The structures were of two main types, one short and thick with few curves, the other longer and thinner and with a wavy rather than a spiral outline. Latterly, some of the finer type were seen being detached from blood-platelets, and some of the shorter forms appeared to be formed from the red cells after these had been anchored to the slide and had thereafter been freed by currents in the film. In view of these findings and in complete agreement with Dr. Thomson's conclusions, there appeared to be no adequate grounds for relinquishing the previously held belief that blackwater fever is dependent on previous malaria. Indeed the records of cases of this disease occurring in Nigeria during 1923, continue to add proof to the hypothesis.

Reports of only twelve cases were received but five or six others occurred details of which for various reasons have not been furnished.

The various data have been analysed as in previous years and the salient features are herewith presented. All the patients were male adults of British birth. Seven cases occurred in the Northern Provinces, four in the Southern Provinces and one in the British Cameroons. The towns in or near which the patients fell sick are Jos three, Onitsha two, and Ahoada, Bamenda, Ibadan, Ibi, Kaduna, Kano and Zaria, one case each.

The months in which the disease was noted are January, February, March two cases, April, June three cases, August two cases, September and October.

The age of the patient was twenty-four years (two cases), twenty-eight years (two cases), twenty-nine years, thirty-three years (two cases), thirty-four years, thirty-eight years, forty-five years, forty-nine years and fifty-five years.

Six were Government Officials, three belonging to the Provincial Administrative Department, and three engaged on railway work. Of the non-officials two were in the tin-industry, three followed mercantile pursuits and one, banking.

All the individuals had considerable previous tropical experience, except in one case, as is shown in Table I.

TABLE I.

No.	Total time in Nigeria.	Period resident since leave.	Period in other parts of the tropics.
1	4 years ...	11 months ...	None.
2	17½ months ...	17½ months ...	Rhodesia, Nyassaland, Congo Belge, 1 year.
3	3 years ...	3½ months ...	None.
4	2 years ...	6 months ...	None.
5	11 years ...	12 months ...	None.
6	3 years ...	16 months ...	Salonika, Turkey, during the war.
7	3 months	None.
8	16 months	India, Arabia, during the war.
9	3 years ...	12 months ...	India, 6 years.
10	10 years ...	2 years ...	None.
11	11 years ...	7 months ...	None.
12	6 years ...	5 years ...	Rhodesia, Portuguese East Africa, 20 years.

There was thus a sufficiently long period of residence in malarious areas for each to acquire a malarial infection. In fact, with the exception of Case (7), there is a definite history of one or more attacks of malaria in all the subjects. As regards the exception, two attacks of dysentery were contracted in the three months' period of his residence in Nigeria, but there was no history of any other illness. The details of each case are to be seen in Table II.

TABLE II.

- Case (1) Six bad attacks of malaria. Often "slight fever" this tour.
- Case (2) Nine or ten attacks of fever this tour. Several in Nyassaland.
- Case (3) Two attacks of enteritis with malarial parasites in blood, this tour.
- Case (4) A number of mild attacks of malaria.
- Case (5) Had no malaria for years.
- Case (6) Many small attacks of malaria.
- Case (7) No history of malaria.
- Case (8) Frequent attacks of malaria.
- Case (9) Two or three small attacks of malaria in last two months.
- Case (10) Exceptionally healthy. Occasional malaria.
- Case (11) Several attacks of malaria, one within 14 days of illness.
- Case (12) Much fever.

As regards quinine prophylaxis, this drug was for the most part neglected. Table III gives particulars.

TABLE III.

- Case (1) Takes 10 grains thrice daily for a few days when he has fever.
- Case (2) 5 grains quinine Hydrochloride daily.
- Case (3) Takes quinine regularly.
- Case (4) Takes quinine Bihydrochloride in varying doses at irregular intervals.
- Case (5) Took no quinine.
- Case (6) 5 grains Hydrochloride, very regularly.
- Case (7) 5 grains quinine irregularly.
- Case (8) 5 grains Hydrochloride, irregularly.
- Case (9) No quinine for one month before illness.
- Case (10) Took no quinine.
- Case (11) 5 grains daily, regularly.
- Case (12) 5 grains regularly for a year previous to illness, sometimes 10 grains.

These Tables (Tables II and III) show clearly that the patients (five, in all) who professed to take quinine regularly as a prophylactic against malaria were not thereby protected.

The possible reasons for this lack of protection are many but the most likely explanations are some looseness in the use of the term "regular", and a neglect of other precautions particularly the use of mosquito boots. In at least one case (Case 3) the inefficiency of the quinine was due to a chronic gastritis which interfered with the absorption of the drug. In the remaining seven cases, quinine was used either irregularly or not at all. It strongly emerges, from a study of the two tables that in eleven out of twelve cases there is a history of malarial attacks and inadequate quinine prophylaxis. It may be inferred that the malarial infection in several cases was inefficiently treated.

The data respecting quinine as a possible precipitant or excitant of the actual condition of hæmolysis are set out in Table IV.

TABLE IV.

Case.	Salt.	Days.	Dosage.			Total.	Last Dose.	Interval.
1	Hydrochloride	2	10 grains in solution twice daily	40 grains	10 grains	15 hours.
2	"	3	10 grains on each of 2 days, 10 grains twice	"	"	4 "
3	?	1	8 grains	8	8	12 "
4	Bihydrochloride	2	30 grains daily	60	?	?
5	"	1	5 grains	5	5 grains	12 hours.
6	Hydrochloride	4	20 grains on each of 2 days, 15 grains, 20 grains	75	10	14 "
7	Bisulphate	1	5 grains and 10 grains	15	10	12 "
8	Hydrochloride	?	?	?	?	6 "
9	?	$\frac{1}{2}$	5 grains, in solution 4 hourly	20 grains	5 grains	8 hours.
10	Hydrochloride	1	10 grains	10	10	12 "
11	"	1	5 grains in solution	5	5	7 "
12	"	1	15 grains in solution	15	15	2 "

In the above table, the third column "Days" refers to the period before the onset of blackwater, during which quinine was being taken. In the fourth column, in cases (2) and (6) the dosage is given from the first day to the last day of its administration. In the last column "Interval" refers to the time which elapsed between the taking of the last dose of quinine and the first appearance of hæmoglobinuria.

It will be seen that in two cases, the total amount of quinine taken within twenty-four hours of the appearance of blackwater, was 5 grains. In the first of these the patient was not in the habit of taking quinine, and in the second, it was the usual daily prophylactic dose.

A definite history of previous attacks of blackwater fever was obtained in one case only, Case (12), one attack having occurred in 1902 and a second in 1903, both whilst the patient was in Rhodesia. In Case (2), however, there was information that whilst on active service in Russia during 1916, there was an illness lasting two weeks during which "Red water" was passed and jaundice was noted but no rise of temperature. He had then not been previously in the tropics.

There was complete recovery from the present illness in both of these cases.

The premonitory signs and symptoms of the disease vary in the different reports. In some there was a period of malaise, which was usually attributed to malaria and led to the taking of quinine. This period varied from one to four days, but in two cases it had been a matter of weeks.

In Case (1) the patient had been taking 10 grains of quinine twice daily for two days before the onset of hæmoglobinuria, so that presumably he had felt out of sorts.

The history is similar in Case (2). There was fever for two days, for which quinine was taken.

In Case (3) a long period of gastritis with vomiting and diarrhoea probably masked any prodromata.

The previous history could not be obtained in Case (4), as when the patient was reached after some days' travelling, he was delirious and his illness ended fatally.

Somewhat similar circumstances explain the lack of information in Case (5).

In Case (6) an attack of "fever" came on four days before the onset of blackwater, and the patient appeared to have completely recovered from this during the morning of the day in the evening of which hæmoglobinuria occurred.

An "out of sorts" feeling preceded by three days the appearance of blackwater in Case (7) and on the actual day before, the patient thought he had a "touch of sun."

In Case (8) there are no notes as regards onset.

The patient in Case (9) had been in hospital under treatment for malaria for two days before hæmoglobinuria set in.

In Case (10) there was malaise on the previous day.

An attack of fever a fortnight before, had left the patient in Case (11) "not feeling well."

In Case (12) the patient had felt ill for weeks.

The course of the illness also varied within fairly wide limits, apart altogether from the occurrence of remissions or relapses. In most instances there was a well-marked rigor usually preceding but sometimes following the appearance of blackwater. Vomiting took place in most, but not in all; it was mild in some and severe and protracted in others. Diarrhoea occurred in a few cases, usually early in the attack. Jaundice was noted in practically all, mostly on the first day of the actual illness.

Enlargement of the spleen and tenderness over the right hypochondriac area were observed in more than half of the cases. Headache was a frequent symptom and loin pains were less commonly complained of.

A temperature chart was supplied in ten cases. As it is not possible to reproduce these, the bare figures are given, the highest temperature for each day only being noted.

Case (1) 1st day 101·4° F., 2nd 101° F., then normal.

Case (2) 2nd day 103° F, 3rd 100° F, then normal.

Case (5) 1st day 103·4° F, 2nd 102·4° F, 3rd 100·4° F, 4th 100·2° F, 5th normal, 6th 100° F, 7th 102° F, 8th 100·2° F, 9th 105·8° F, 10th 102·4° F, 11th normal, 12th 100·4° F, 13th 102·4° F.

Case (6) 1st day 99·8° F, then normal.

Case (7) 1st day 103° F, 2nd 101·4° F, 3rd 101·6° F, then normal.

Case (8) 1st day 103·6° F, 2nd 102·8° F, 3rd 102·8° F, 4th 101·2° F, 5th 102·4° F, 6th 101·4° F, 7th 100·6° F, 8th 100° F, 9th 99·4° F, then normal.

Case (9) 1st day 102° F, then normal.

Case (11) 2nd day 102° F, 3rd 101° F, 4th 103° F, 5th 100·2° F, 6th 100° F, 7th 100·8° F, 8th 100·8° F.

Case (12) 6th day 104° F, 7th 102·6° F, 8th 101·4 F, 9th 100·8° F, 10th 100·8° F, 11th 101° F, 12th 99·6° F, 13th 100° F, 14th 100° F, then normal.

In Case (10) the patient was first seen on the 5th day of illness and from then onwards until his death on the 7th day the temperature varied between 97·2° F and 98·2° F.

A study of these data shows that in two cases the temperature became normal on the second day, on the third day in one case, on the fourth in two cases and on the tenth and fifteenth day each in one case. There was a relapse in Cases (5) and (11), in which the febrile state was prolonged.

The duration of hæmoglobinuria, in cases in which there was neither remission nor relapse and in which there was no suppression, was twenty-four hours (Cases (6) and (9)) forty-eight hours, (Cases (3) and (7)) sixty hours, (Case (2)) and ninety-six hours (Case 8)). Relapses occurred in four cases. In Case (1) the first period of hæmoglobinuria lasted just over six hours. After a seven hours' interval and following a rigor, the urine was again porter-coloured and it did not clear until thirty-nine hours later. In the interval the temperature had fallen, but it rose again during the relapse. The total period of hæmoglobinuria was forty-five hours, and recovery was rapid. In Case (5), the initial period of passing black water was seventy-two hours. The urine cleared gradually but remained "smoky" until the ninth day, when it again became very dark. During the ensuing five days hæmoglobinuria was persistent and the patient died on the thirteenth day of illness. This case might be described as one showing a remission. The temperature gradually fell from the second day to the sixth day, when it was normal but it immediately rose again regaining normal on the eleventh day and fluctuating thereafter until the thirteenth day. In Case (11) the initial hæmoglobinuria completely disappeared after ninety-six hours. The urine remained clear for forty-eight hours, but became dark red again and remained so for thirty-six hours, when death took place. There was some abatement of the fever when the urine became clear, the temperature then being about 101° F and it showed no rise when the relapse occurred. A series of relapses characterised Case (12). The first period of hæmoglobinuria lasted thirty-six hours. Forty-eight hours later the red colour returned and persisted for twenty-four hours. At the end of the sixth day of illness, after the urine had been clear for twenty-four hours, there was a relapse lasting seven-and-a-half hours. Two days later the urine was again reddish for four hours. On the tenth day, after a two days' interval of freedom there were two relapses the first lasting four hours in the early morning and the other nine-and-a-half hours in the latter part of the day. And again on the following day two relapses occurred one lasting twelve hours and the other about two hours. The final relapse was noted at the end of the twelfth day but only one coloured specimen was passed, and progress was steadily maintained thereafter. The temperature was febrile during all this time but was steadily falling and the normal line was reached on the day after the last relapse occurred.

As already noted death occurred in two of these relapsing cases, Nos. (5) and (11).

In the two cases, in which suppression occurred and death followed, the hæmoglobinuria was obvious for the first twenty-four hours in Case (4) and thereafter no urine was passed. In Case (10) hæmoglobinuria was observed on the morning of the first day. Thereafter no urine was passed until the fifth day when two drachms of port-wine urine were passed, after which there was complete suppression. The illness lasted seven days in Case (4) and six days in Case (10).

Albuminuria, as a rule cleared up within twenty-four hours of the disappearance of the hæmoglobinuria but in Case (1) it persisted forty-eight hours, in Case (6) for seventy-two hours, and for six days in Case (8), after the urine had regained a normal colour.

The blood was examined in nine cases. The results are shown in Table V from which it will be seen that the parasite of subtertian malaria was found in only one instance, Case (8) and that by the medical officer in attendance.

Smears were received at the Medical Research Institute from seven of the cases.

TABLE V.

500 leucocytes counted for differential } counts.
250 polymorphs counted for Arneth

Case.	Day.	Para.	Pig.	P.	S.	L.	M.	E.	T.	Ma.	My.	Ery.	Vac.	Nor.	Meg.	I.	II.	III.	IV.	V.
1	1st ...	0	0	69.4	3.8	1	20.8	0.2	3.6	0	1.2	1	1	0	0	79.6	16.8	3.6	0	0
	2nd ...	0	0	64.4	11.4	3	16	0	3.2	0.2	1.8	1	3	0	0	77.2	17.2	5.6	0	0
	3rd ...	0	0	61	14.4	3.8	15.4	0.6	2.2	0.6	2	0	2	3	0	65.2	26.8	7.6	0.4	0
2	1st ...	0	0
	2nd ...	0	0	58.4	21	4.6	13.6	0	2.2	0.2	0	0	6	0	0	71.6	24.4	4	0	0
	3rd ...	0	0	62.2	11.4	2.6	19.2	0	3.8	0	0.8	0	0	0	0	45.2	39.6	14.8	0.4	0
5	4th ...	0	0	66.6	17.6	4.4	7.6	0.6	2.6	0	0.6	0	0	0	0	57.6	34.4	7.6	0.4	0
	5th ...	0	0	52.6	9.8	4.2	20.6	4	2.4	0.2	6.2	0	0	3	6	54.8	33.6	11.6	0	0
	9th ...	0	0	65	7.6	3.6	19	0.2	3.2	0	1.4	0	0	0	3	64	30.4	5.2	0.4	0
6	10th ...	0	0	81.4	6.4	1.8	6	0.6	3.4	0	0.4	1	0	0	0	62.8	29.6	7.6	0	0
	1st ...	0	0	76.2	5.8	1.6	12.2	1.2	2.6	0	0.4	0	0	0	0	70.4	23.2	5.6	0.8	0
	2nd ...	0	0	70.6	7	2	11.8	4	2.8	0.2	1.6	0	0	0	0	72	22	5.2	0.8	0
7	3rd ...	0	0	68	7	1.8	14.6	4.8	2.6	0.6	0.6	0	0	0	0	69.6	24	6	0.4	0
	4th ...	0	0	59.6	14	4.6	10.4	4.4	1.8	0.4	4.8	1	0	0	0	54	30	13.2	2.8	0
	5th ...	0	0	63.8	11.8	2.6	12	4.2	2.2	0.2	3.2	0	3	0	0	48	28.8	18.8	4	0.4
8	2nd ...	0	0	64.8	18.2	3.8	11.6	0	1.6	0	0	0	0	0	0	79.2	16.8	4	0	0
	1st ...	+	+
	5th ...	+	+
10	5th ...	0	0	59.8	15.2	2.2	16.6	1.2	0
	2nd ...	0	0	76	9.2	2.2	11.6	0	3	0	2	0	2	1	0	56	26	15.2	2.4	0.4
	3rd ...	0	0	67	10	3.4	16.4	0	0.8	0	0.2	0	2	0	0	61.2	30.8	7.6	0.4	0
11	4th ...	0	0	62.8	13.2	4.4	15.8	0	2.2	0	1	0	15	0	0	49.6	29.6	17.6	3.2	0
	5th ...	0	0	63.4	18.6	3	7.4	0.4	2.4	0	1.4	0	4	1	0	50.8	31.6	15.6	2	0
	6th ...	0	0	67.2	12.6	4.4	9.6	2.2	5.8	0	1.4	0	7	1	0	59.2	28.4	9.6	2	0.8
12	6th ...	0	0	48.4	8.8	4.8	36	0.4	2.2	0	1.8	0	0	0	0	50.4	29.2	16.4	3.6	0.4
	14th ...	0	0	43.6	20	7.2	23.2	0.8	2.8	0	2.4	0	6	1	0	64	22	9	5	0
																64.4	24.4	11.2	0	0

“Day” refers to onset of hæmoglobinuria. Para=Parasites (subtertian malaria). Pig=Pigment. P=Polymorphonuclear neutrophils. S=Small lymphocytes. L=Large lymphocytes.
M=Mononuclears. E=Eosinophils. T=Transitionals. Ma=Mast cells. My=Myelocytes. Ery=Erythrocytes. Vac=Vacuolated mononuclears. Nor=Normoblast.
Meg=Megaloblasts.

The Roman numerals refer to Arneth's divisions.

RELAPSING FEVER.

Relapsing fever made its reappearance in Lagos during the year. The sole previous authenticated record of its occurrence was in 1910, when, on July 23rd, spironemata were found, at this Institute, in the blood smear from a native patient in the Colonial Hospital at Lagos. It is true that on rare occasions since that date, cases of "Relapsing Fever" have been reported both in Europeans and in natives, from the Northern as well as from the Southern Provinces of Nigeria, but the diagnosis was not based on findings at this laboratory. It is possible that what was really meant was the relapsing type of malarial fever.

Fortunately the outbreak in 1923 was a small one. The first case was diagnosed on 11th July, the second on 12th September, the third on 13th September, the fourth on 15th September, the fifth on 19th October, the sixth on 9th November and the seventh on 27th November. Five of these seven cases were diagnosed during life, and all recovered under treatment in hospital. The remaining two were both admitted to hospital in a moribund state and the diagnosis was made from post-mortem findings. Cases (1), (3) and (4) all received a single dose of Salvarsan. Cases (5) and (6) were given a single dose of Novarsenobillon with happy results, although in Case (5) it was not administered until a relapse had occurred.

Excluding Cases (2) and (7) in which death took place a few hours after admission to hospital, the clinical course of the disease presented no unusual features. Prostration was marked and there was intense headache, with general body pains. The spleen was moderately enlarged in all the cases.

In connection with the much larger outbreak of the disease in the Gold Coast, it is interesting to note that five of Lagos cases occurred in "Zabarumas," or, as they are called in the Gold Coast Report "Zabramahs," a people inhabiting the hinterland to the north of Nigeria. The first case, however, was that of a labourer belonging to the Public Works Department, who for five years previously had never been out of Lagos.

The causative organism, a Spironema, was readily found in all the cases. In five instances, only one smear was obtained, in one case blood films were taken on three successive days and in another, films were made on four successive days. In its morphology and in its behaviour in laboratory animals, the spironema agrees closely with that described in the Gold Coast epidemic. Twenty organisms in each smear, with the exception of one case in which only a very few spironemata were found in a spleen-smear made post-mortem, were drawn with the aid of the camera-lucida and afterwards measured by compass. The details of these are set out below.

Case (1). Yesufu. Male. Age about thirty years. Labourer. The shortest was 13·5 microns, the longest 27 microns and the average length 17·5 microns.

Case (2). Isa. Male. Age about thirty years. Carrier. The shortest was 7·5 microns, the longest 19·5 microns, and the average length was 13 microns.

It should be noted that the smear from which these measurements were taken, was made from the brain, post-mortem.

Case (3). Yahaya. Male. About twenty-two years of age. Carrier.

13/9/23. Shortest 13 microns, longest 29·5 microns, average 20 microns.

14/9/23. Shortest 12 microns, longest 23·5 microns, average 16 microns.

15/9/23. Shortest 11 microns, longest 26 microns, average 19 microns.

Case (4). Brimah. Male. Age about twenty years. Carrier.
The shortest was 10 microns, the longest 25 microns and the average length was 16 microns.

Case (5). Dogo Yaro. Male. Age about thirty-five years. Carrier.

26/10/23. Shortest 13·5 microns, longest 27 microns, average 20 microns.

27/10/23. Shortest 11 microns, longest 29 microns, average 18·5 microns.

28/10/23. Shortest 13 microns, longest 33 microns, average 19 microns.

29/10/23. Shortest 14·5 microns, longest 31 microns, average 21·5 microns.

Case (6). Abudu. Male. Age about twenty-two years. Carrier.
The shortest was 11·5 microns, the longest 31 microns and the average length was 21 microns.

In addition to these, smears from two other cases of the disease were kindly sent by Dr. Cauchi. One of the cases occurred at Kaduna in November. The shortest organism was 13·5 microns, the longest 27 microns and the average length was 19·5 microns: The other case occurred at Kontagora in December. The shortest spironema was 14 microns, the longest 30 microns and the average length was 20 microns. The breadth of the organism in all the cases was about 0·3 microns. In Cases (3) and (5) it was noted that coiled, looped or bent forms were numerous on the second and third days. No attempt was made to count the spirals. In such forms as were observed to be dividing, the process was always by transverse division, although occasionally the two halves were bent back into such close apposition as to simulate longitudinal division. The organism tapered gradually at both extremities to a fine point. In fresh blood, under the microscope, the movements noticed were of two kinds, one a very rapid darting to and fro, impossible to follow, the other in which a fine tremor occurred with more or less rotation in the long axis. The spironemata stained readily, were well shown up with Giemsa and were particularly prominent with Fontana.

Cultivation. 10 c.c. of citrated blood from Case (3) and a similar quantity from Case (4) were incubated at 37°·5 C but no growth took place. At the end of seventy-two hours groups of motionless spironemata were found under the microscope, which was an interesting result, inasmuch as both patients had received an intravenous injection of Salvarsan, a few hours previous to the collection of their blood. On the fourth day, two c.c. of the culture from Case (3) were given intraperitoneally to monkey No. 1, and a similar amount from Case (4) was given by the same route to monkey No. 2. Neither of these animals showed any reaction, and, in daily examinations of their blood during the ensuing fortnight, no spironemata were seen. However, five weeks later, along with four other monkeys, they each received 2·5 c.c. of blood intraperitoneally from Case (5). The two previously inoculated monkeys (*Cercopithecus tantalus*) showed no reaction whilst the four fresh monkeys (also *Cercopithecus*) developed an infection rapidly. Very possibly, therefore, the previous injection served as a protective vaccination. The other attempt at cultivation was more successful. The medium used was that recommended by Wenyon for the cultivation of protozoa (fresh rabbit's blood in saline with a small percentage of agar, the mixture having a definite P.H.), and as the patient, Case (5) had received no treatment, growth readily took place at a temperature of 37°·5 C in the incubator. The tubes rapidly became contaminated, however, after several examinations.

Animal transmission. Three guinea-pigs were inoculated intraperitoneally with 1 c.c. citrated blood from Case (3), two guinea-pigs were similarly treated from Case (4), and, as above noted, monkeys No. 1 and No. 2. The results were negative in all. Monkeys Nos. 3, 4, 5, and 6 were inoculated intraperitoneally with 2.5 c.c. of citrated blood from Case (5). At the same time, two fresh guinea-pigs received an injection by the peritoneal route, of 2 c.c. blood from the same case. Monkey No. 3 was positive one day later, and two days later monkeys Nos. 4, 5 and 6 were also positive. In all four the injection lasted four days, monkey No. 3 clearing up one day before the others. No relapse was observed in any although the blood was examined daily for twenty-one days after the primary infection. The guinea-pigs did not at any time exhibit signs of illness nor were the organisms found in the blood.

The spironemata in the four monkeys were also measured, as in the human cases, and the figures are given below.

Monkey No. 3 inoculated 26/10/23 from Case 5.

27/10/23. Only one spironema seen in blood smear.

28/10/23. Only two spironemata seen in blood smear.

29/10/23. Shortest 12.5 microns, longest 31 microns, average 20 microns.

30/10/23. Shortest 13 microns, longest 26.5 microns, average 19 microns.

Monkey No. 4, as No. 3.

28/10/23. One spironema seen in blood smear.

29/10/23. Shortest 15.5 microns, longest 32 microns, average 22 microns.

30/10/23. Shortest 11 microns, longest 28 microns, average 19 microns.

31/10/23. Shortest 13 microns, longest 31 microns, average 18.5 microns.

Monkey No. 5 as Nos. 3 and 4.

28/10/23. Shortest 13 microns, longest 26.5 microns, average 19 microns.

29/10/23. Shortest 14.5 microns, longest 28 microns, average 20 microns.

30/10/23. Shortest 13.5 microns, longest 29 microns, average 20 microns.

31/10/23. Shortest 13 microns, longest 22.5 microns, average 17 microns.

Monkey No. 6, as Nos. 3, 4 and 5.

28/10/23. Two spironemata seen in smear.

29/10/23. Shortest 15 microns, longest 32 microns, average 24.5 microns.

30/10/23. Shortest 13 microns, longest 34 microns, average 22 microns.

^{3/}30/10/23. Shortest 16 microns, longest 32 microns, average 23 microns.

It will be seen that although the average length of the organism in the human cases and in the monkeys varies between 13 microns (in a human case, post-mortem) and 24.5 microns (in monkey No. 6), yet considering the small number of spironemata measured, the averages agree fairly closely.

Experiments with lice and bugs. On 15/9/23 eight lice (*Pediculus humanus*) which were recovered from the room in which the patient in Case (3) slept, were fed on two guinea-pigs. The animals remained healthy. On 17/9/23, thirteen lice obtained from the clothing, in Case (4) were fed, some on a monkey, some on a guinea-pig. No infection resulted. On 18/9/23 all of these twenty-one lice were ground in a mortar, with a small amount of normal saline, and the material was well rubbed into a scarified area on the abdomen of a monkey and of a guinea-pig. Neither of these animals was infected thereby, although a few spironemata were seen in the ground-up material under the microscope. On 25/9/23 four bugs (*Cimex rotundatus*) obtained a week previously from the room in which Cases (3) and (4) occurred, were crushed in a mortar and the material rubbed into a scarified area on the abdomen of a monkey. A few structures resembling the spironema were seen in this material under the microscope, but it failed to infect the animal. On 30/10/23, fifty-nine lice, obtained locally by one of the Institute labourers were offered a feed on monkeys Nos. 3 and 4, both of which were then showing large numbers of spironemata in the peripheral blood. Twenty-four lice fed on monkey No. 3 and twenty-one on monkey No. 4. Fourteen refused to feed. Each louse was then placed on a small piece of paper in separate plugged test-tubes and kept in the dark at laboratory temperature. On the following day 31/10/23 there were three deaths in Batch C, that is those which had not fed. The remaining eleven readily fed on monkey No. 5 which on that day showed numerous spironemata in the peripheral blood. Batch A consisting of the twenty-four lice which had fed on monkey No. 3 had a death roll of one, and the remainder took a blood feed from a clean guinea-pig. Batch B containing twenty-one lice which had fed on monkey No. 4 which also had one casualty, were offered a feed on a clean guinea-pig, and the twenty survivors quickly distended themselves with blood. During the night all three batches were kept at laboratory temperature and on the following morning, 1/11/23 the living ones again greedily fed from a guinea-pig. The deaths in Batch A numbered six, those in Batch B, four, and there were no losses in Batch C. However, it was deemed advisable in view of the comparatively cold nights to keep all the insects in the incubator, in the hope that a fair percentage would be alive at the end of seven to ten days. The results however, of this change, were disastrous. On the morning of 2/11/23 not a live louse remained and the experiment ended abruptly. No further opportunity has presented itself of improving on and completing this experiment as no fresh case of relapsing fever occurred.

LEPROSY.

The close proximity to the Medical Research Institute, of a small Leper Asylum (containing sixteen to twenty inmates) has stimulated an interest in the treatment of the disease which has been manifested in the Annual Reports from 1915 onwards. Previous to that year, the Medical Officers in charge of the Asylum had relied mainly on the crude Chaulmoogra oil and they had also given Deycke's Nastin treatment an extended trial.

During 1915 the late Dr. H. Sinclair Coghill used Salvarsan on two lepers, with some benefit and during 1916 he administered Heiser's treatment (Chaulmoogra oil, Camphorated oil and Resorcin) with really encouraging results. The only objection to the use of this mixture is that as the dosage increases, it becomes a somewhat bulky amount to inject intramuscularly and the patience of the leper soon gives way. For this reason, and in the belief that the curative principle of the crude oil is more concentrated in the extract, Sodium Gynocardate, recommended by Rogers was used in 1917 and 1918, both intramuscularly and intravenously. In the latter half of 1918 Atoxyl was given as well as Gynocardate to several of the patients but there was no evidence of better results in these. On the whole, the Gynocardate treatment was

superior to Heiser's, as regards the rate of improvement, and there was not the same objection by the patients to its continued use. In the following year, Roger's method was adhered to, combined with the use of Nastin B.I. This latter preparation did not appear to hasten or aid the healing process. By the end of 1919 the disease was, to all appearance definitely arrested in five cases, greatly ameliorated in six, and without any restraining effect in one. This last was a recent and very acute case.

During 1920, Potassium Cupro cyanide, in view of a very favourable report in the Tropical Diseases Bulletin, was given a trial in the last-named case and in two others which had shown improvement with Gynocardate. At the end of three months there was now evidence whatsoever, of benefit, and it was given up. For the greater part of this year, therefore, no special treatment was given. The only drug used was the crude Chaulmoogra oil and the patients were allowed to please themselves as to how much they took and when they took it. Moogrol was then adopted, in the latter half of 1921, at which time, the five patients in which the disease appeared to have been arrested at the end of 1919, still showed no sign of relapse. However there was a severe exacerbation of the disease in two of the six cases which had improved and in the acute case, the condition was still an active one. These three patients and four others recently admitted were given Moogrol intravenously. The result of four and a half months' administration was a distinct improvement in all, particularly in the acute case.

During the early part of 1922 Oscal Stibium was substituted in three of the new cases and Moogrol was continued in the remaining four. In April however, all the cases were put on Harper's treatment (Moogrol Ether and Iodine). This was given at first intravenously, then intramuscularly, and finally, omitting the ether, the Moogrol and Iodine were given in a chalk mixture, by the mouth. The improvement was more or less maintained during the six months of this regime, but in 1923 it was decided to resort again to Moogrol by the intravenous route, with seven patients, five of them old inmates and two new admissions. All showed improvement, in such ways as healing of ulcers, decrease in size and number of tubercles, disappearance of maculæ and improvement in sensation.

The object aimed at is not a rapid cure which appears to be unattainable, but to keep the patients contented and optimistic so that they may be willing to continue the treatment over many months, even years, inasmuch as the disease itself being of a slowly progressive nature the process of cure must of necessity be a protracted one. The advantages of the Moogrol treatment are, besides its specific action on the lepra bacillus, (a) that the amount of the drug necessary to obtain good results is small (2 to 4 c.c.), and therefore it is easily administered with a small syringe and a fine needle, (b) that administration once or at most twice a week is adequate, (c) that no cumbersome preliminary preparation is involved, the boiling of the syringe and needle, and the application of iodine to the skin over the site of puncture being all that need be done, and (d) provided the vein be entered there is no local disturbance and the patient is satisfied. This last is an important practical point, for the Nigerian leper will not long submit to hypodermic or intramuscular medication, and he takes quite a keen interest in the successful puncture of a vein with no swelling left behind.

The following extracts from reports by Medical Officers who have been using Moogrol in outstations, are given.

Dr. W. C. Cobb, D.S.O., reports from Bauchi, 9/1/24.

Case (1) Male, aged twenty-seven years. States four years a leper. Only one lesion, a roughly oval-shaped macule on back, about five inches long, definitely anæsthetic in parts, with edges slightly raised, and much lighter in colour than

the rest of the lesion, which showed a darker area in the middle containing a small patch of scar tissue. Weekly intravenous injections of Moogrol have been given since 8/8/23, the first one $\frac{1}{2}$ cc., six of 1 cc. and fifteen of 2 cc.. After about two months of treatment slight improvement was apparent at one end of the lesion, but this was balanced by a spread at the other. At the present time, the edges of parts of the lesion are probably somewhat less raised than at first; but, considering the normally changeable nature of leprosy patches, the verdict must be that there is no improvement.

Case (2) Male, aged twenty-seven years. States seven months a leper. Faint light-coloured macules on back, chest and abdomen, quite difficult to see unless light from right quarter. Weekly intravenous injections of Moogrol started on 8/8/23. First dose $\frac{1}{2}$ cc. followed by five doses 1 cc, followed by five doses 2 cc. The patient then left prison and disappeared. During treatment the disease progressed regularly and rapidly with the result that the conclusion of treatment found him a well-marked leper. I was glad to see him go as I felt I was doing him harm.

Case (3) Male, aged thirty years. States eight months a leper. Same type as last case but macules more numerous and more evident. Weekly intravenous injections of Moogrol started 31/10/23. First dose $\frac{1}{2}$ cc. second dose 1 cc. followed by eight doses of 2 cc. Up to the present there has been no apparent change, one way or the other.

Case (4) Male, aged twenty-five years. States one year a leper. Numerous well-marked macules, type similar to that in Case (1). Started treatment same date as Case (3), dosage the same, result the same.

Dr. A. Gaston reports from Kano, 21/1/24, as follows:—

Three lepers are being treated at the present time. They are the anæsthetic type of leprosy. One of them has had the disease for twenty years, and has had seven injections of Moogrol, but not much improvement has been noticed. The other two state that they have had the disease for two years. They are getting weekly injections of Moogrol. They have only had two injections so far and not much improvement has been noticed yet. These three lepers are all prisoners. I find that Moogrol does a lot of good in the anæsthetic form of leprosy which is the only form I have treated with this drug.

After six injections I found that the anæsthetic patches had almost completely disappeared and the patients felt much better. Some of them had a slight reaction accompanied by a slight rise in temperature and a little induration around the seat of injection, but this soon passed off.

Dr. W. E. S. Digby reports, 5/1/24, from Maiduguri. Six lepers suffering from mixed leprosy but with the nodular form more predominant, were treated with Moogrol injections, commencing 20th September, 1923. Their names were:—

(1) Mustafa Zavami. (2) Momadu Wanzam. (3) Mallam Hashim. (4) Momadu Mandara. (5) Osuman. (6) Momadu Arimi.

The injections were given intramuscularly in the gluteal region, increasing by 1 cc. each week till, on October 25th, each was receiving 6 cc. There was marked improvement in the nodules of (1) who subsequently died 21st December from Broncho-pneumonia. A more marked improvement was noted in the nodules of (2), who refused further treatment after 13th December. In the case of (3) running sores and ulcers dried and healed up, but further treatment was refused after 13th December. In the cases (4), (5) and (6) no improvement was noticed, but each individual was emphatic in saying his general health

was much improved. They all refused further treatment (4) after 13th November, (5) after 6th December and (6) after 15th November. Two other lepers with macular leprosy attended for injections for three weeks and then refused further treatment.

Dr. N. A. Dyce-Sharp reports, 24/1/24, from Kaduna as follows :—

This drug (Moogrol) has been tried on three patients during the past six months. The period is too short to warrant a definite statement on the value of the drug, but it appeared to be of considerable benefit and all three patients appreciated it.

Dr. G. H. Gallagher reports, 21/1/24, from Bamenda. S. W. Male, aet thirty, Soldier, Native of Sokoto, Anæsthetic leprosy, two years. Four intravenous and thirty intramuscular injections of Moogrol rendered the anæsthetic areas thoroughly sensitive, but there is still an ulcer on the foot. Patient states his general health is improved.

M. B. female, aet, ten. Native of Bafut, Bamenda, admitted for treatment. There was ulceration in both feet, and extensive anæsthetic areas both legs. There was absorption of the metacarpal bone of index finger. Twenty intramuscular injections of Moogrol were given. The patient discharged herself after three months. The ulceration had then all cleared up, but the anæsthetic areas remained.

CALABAR SWELLINGS.

Information regarding ten cases of this affection has been obtained, bringing the number of European cases up to forty, and the number of female sufferers up to five.

As with the previous cases (Annual Report 1922, pages 2-8) the infection was contracted in Nigeria or in British Cameroons.

The length of time which elapsed between the first exposure to infection and the first appearance of signs of the disease is given as one year or less in five instances. The shortest period is three months, the next four months and then seven months, nine months and one year. The other periods are two years, three years, six years, seven years and ten years.

Swellings occurred in nine cases, and were absent in one.

The worm has appeared in the eye in six cases.

The outline of the worm has been seen beneath the skin in four cases.

Embryos of *Filaria loa* were demonstrated in the blood in three cases, but in three instances the blood has not been examined.

The swellings occurred in the upper limbs in all cases, and in five cases the upper limbs only were involved. They occurred also in the legs in three, and in the neck, head, tongue and eyelids in one.

Swellings arose in sequence in four cases, and were multiple also in four. They began during the day in two, during the night in two, and either day or night in five.

The duration of the swellings and the period of freedom depended on the stage of the infection. In the early cases, the swellings persisted longer and the period of freedom was shorter than in the older infections.

In three instances the swellings have been absent for a long period with the probability that the infection has died out.

Case (37) Duration of illness nine years. Swellings absent one-and-a-half years.

Case (38) Duration of illness fourteen years. Swellings absent four years.

Case (40) Duration of illness thirteen years. Swellings absent three years.

In three cases the swellings are becoming more severe and more frequent, with shorter periods of freedom. These cases are (31) illness of one year, (32) illness of fifteen years (35) illness of one year.

As regards Case (32) this patient is still in the area where the original infection was contracted, and it is highly probable that there has been re-infection.

In Case (33), after seven years the swellings are less severe and less frequent.

In Case (34), after one-and-a-half years there is little change.

In Case (39), the swellings had appeared for the first time two days before the report was made. The patient remembered at least two bites from Chrysops, both on the same hand, one five months and the other two months previously.

The sensation of the swellings is described as a tenseness or tightness, or stiffness in seven cases and as a dull pain in two cases.

The worm occurred in the eye in five cases in which swellings also were noted. In four of these the swellings were the first sign, and in one they were contemporary. In three instances the worm had only once appeared in the eye. In Case (40), in which there were no swellings, the infection was contracted 20 years ago. For the last eight years, no worm has been seen either in the eye or under the skin. In this instance and also in Cases (39) and (37) one or more adult worms had been removed from the eye. The cases in which the worm could be traced moving just under the skin are all of old standing, (32) fifteen years, (37) fourteen years (39) thirteen years and (40) twelve years.

The blood has not been examined for embryos in Cases (31), (34) and (39). The examination was negative in Cases (32), (33), (35) and (38). In Cases (35) and (38) the infection was recent, a few days in (38) and one year in (35). The three cases in which embryos were present or had been demonstrated were all old-standing.

As regards the cases reported in 1922, fresh information has been collected from sixteen. Of the remainder, two were regarded as cured in that report. Cases (9) and (13). One has died (Case (16)), and the cause of death has not been ascertained.

Two cases cannot be traced and replies are awaited from nine.

Taking the sixteen cases, in their order, embryos have appeared in the blood in Case (1), the swellings are less severe, the period of freedom is longer and the worm has only once appeared in the eye. In Case (4) also, embryos have appeared in the blood, but the swellings although not so widespread and so numerous are more lasting. Several times a worm has visited the eye. In Case (5), a worm has been seen under the skin of the forearm but none has visited the eye, and no embryos have been seen in the blood. The swellings are of shorter duration and there is a longer period of freedom.

Case (6) is worthy of note. A year and a half ago Dr. Parkinson, Surgical Specialist at Lagos gave the patient a course of Stibenyl, intravenously. All signs of infection have since been absent.

In Case (7) a worm has appeared once in the eye. The swellings are fewer and of shorter duration and the period of freedom is longer. Embryos have not been found in the blood.

In Case (8) the only change is that the period of freedom from swellings is longer.

In Case (10) a worm has frequently appeared in the eye, and there is no change in the conditions as regards the swellings.

In Case (12) there are still embryos in the blood, the worm visits the eye more frequently, and the swellings are more often multiple.

In Case (15) embryos have not been found although repeated examinations have been made. The swellings cause much less disturbance and occur only occasionally, the worm is less often seen in the eye but has more frequently been noted on the chest, back of hand, temple, nose, forehead and eyelid.

In Case (17) the swellings have been very infrequent, a worm has not been seen or felt in the eye, and no embryos have been found in the blood.

In Case (18) there have been no swellings since last report (18 months) and a worm has not visited the eye.

In Case (24) a worm has not again appeared in the eye, the swellings only last a day or two and there is a much longer interval of freedom. Embryos were not found in the blood on this occasion.

In Case (25) there have been no signs of infection.

In Case (27) there have been no swellings for nearly two years, and the last visit to the eye occurred seven years ago.

In Case (28) there have been no signs of the infection since the last report.

In Case (29), the worm has not been seen in the eye since last report (nearly two years) and no other signs have been noted.

FILARIAL EMBRYOS FROM THE SKIN.

The results obtained by Dr. Macfie and Dr. Corson on the Gold Coast, in 1922 regarding the presence of embryos of *Onchocerca volvulus* in the skin and their finding, during their research, a hitherto undescribed embryo, prompted an investigation on the same lines, in Lagos.

Dr. C. J. H. Sharp, who, at the time was in charge of the clinical laboratory at the Colonial Hospital collected the material, and sent his positive findings to the Institute. The method adopted was similar to that used in Accra, a small piece of skin, similar to that used in the Reverdin method of skin grafting, was snipped off and teased out in saline.

Fifty-five natives were thus examined in Lagos and embryos were found in six. In two of these in addition to the embryos of *O. volvulus*, the embryos described by Macfie and Corson as *Agamofilaria Streptocerca* were observed. In one of these cases only two of the latter were found amongst twenty examples of the former. In the other case, there were three specimens of *A. streptocerca* and only one of *O. volvulus*.

As regards the embryos of *O. volvulus* the following table gives the measurements obtained in each case. The specimens were simply dried in the air fixed in Methyl Alcohol and stained either with Giemsa or Ehrlich's Acid Hæmatoxyline. They were drawn to scale with the aid of the camera lucida and measured with a pair of compasses.

MEASUREMENTS IN MICRONS.

Case.	Number Measured.	Greatest Length.	Smallest Length.	Average Length.	Greatest Breadth.	Smallest Breadth.	Average Breadth.
1	29	320	240	281	7	4	5
2	26	322	245	283	5	5	5
3	20	325	230	271	6	4	5
4	16	279	215	255	6	4	5
5	3	297	282	288	5	5	5
6	1	306	306	306	6	6	6

The slight thickening behind the cephalic cone at the beginning of the nuclear column, given as a characteristic feature by Stephens and Yorke in Byam & Archibald's "The Practice of Medicine in the Tropics", Vol. III, 1923 page 1,952, was observed in a very small minority of the total number of eighty-five specimens examined. Similarly, with another characteristic, noted on the same page of the same book, as regards the two first nuclei of the gut cells, in hæmatoxylin-stained preparations, it was found that one nucleus in advance of the others was a much more common occurrence, than two so placed. The anterior V spot or first break in the column of nuclei is a very prominent one, indeed the only definite one. It is situated, on the average at 60 to 65 microns from the anterior extremity. The column of nuclei begins at about 10 microns from the head end, and ceases at about the same distance from the caudal extremity.

In no single instance was the tip of the tail-end flexed.

In all cases the G I cell was large and easily seen.

Observations based on examination of the five specimens of *Agamofilaria streptocerca*, agreed with the description given by the two discoverers, Macfie and Corson, except that in no instance was the body straight or nearly so, nor was the posterior extremity curved like the handle of a walking stick except in one case.

The measurements are, in microns.

Length.	Breadth.	1st break from head-end.	2nd break from tail-end.
230	3	60	27
225	3	59	29
212	4	58	30
197	4	60	28
212	4	59	30

The column of nuclei at the head end begins as a single row of from 6 to 10 nuclei. The clear area at the anterior end measures from 4 to 5 microns in length. The body of the worm tapers gradually from two-thirds of the total length to the tail end. The column of nuclei reaches to the extreme tip, the last eight to ten being in a single row. The cuticle is distinctly striated.

It may be added that the cases were chosen at random and that in no instance was there any appearance of lichenification or other abnormality of the skin.

EXPERIMENTS ON THE TRANSMISSION OF ACANTHO-CHEILONEMA PERSTANS.

On 10th October thick blood smears from forty-one prisoners and thirty-one hospital inmates were taken, between the hours of 10.30 and 11.30 a.m. These were afterwards dehaemoglobinised, fixed and stained. On examination, in the former category (prisoners) one was found with a pure perstans infection (Case J) and one with a mixed infection of perstans and loa. Nine others harboured loa only. In the latter category (hospital patients) a pure perstans (Case T) and a pure loa infection were noted.

On 11th October, between the hours of 10 and 11.30 a.m. seventy-two *Mansonioides africana* ♀ ♀ were offered a feed on the prisoner J with a pure perstans infection. Seven insects fed, and they were put into separate test-tubes. A blade of grass was inserted into each tube along with a small piece of sugar, and the cotton-wool plug was moistened with water. The insects were kept in the dark. On the fourth day thereafter one was killed and dissected. One larvæ was found in the thorax, but it was very slightly larger than the blood form. On the fifth day one insect was killed, and another was found dead. No larvæ were found. The same result followed the dissection of the remaining four, one on the sixth, one on the seventh, one on the eighth, and one on the ninth day.

On 12th October thirty-one *M. africana* were offered a feed on hospital patient T. between 11 a.m. and noon. Only one mosquito fed. Between the hours of 3 and 4.30 p.m., forty-eight *M. africana* were offered a feed on the same patient. None fed. Between 6.30 and 7.30 p.m. the same insects were again offered an opportunity of feeding on Case T. and two took advantage. On the following day, 13th October, fifty-six *M. africana* were offered a feed on the same patient between 10 a.m. and 11 a.m. Three fed. Fifty-two were offered a feed between 6 p.m. and 7 p.m. on the same patient on the same day and one fed. Of the insects feeding on Case T., three died within twenty-four hours. Embryos were present in the gut but not elsewhere. A fourth died on the second day. No developmental forms were found on dissection. On the third day, two were found dead. Three forms were found in the thorax of one but no development had taken place, and the other showed no signs of infection. The last of the seven insects was killed on the fourth day, but the results of examination after dissection were negative.

DISSECTION OF HOUSE FLIES.

During September and October fifty-two *Musca domestica*, seven *Lucilia* sp and three *Fannia* sp were dissected in a search for human intestinal protozoa.

No amœbic cysts were found but in one specimen of *M. domestica* numerous *Strongyloides* ova and larvæ were seen. *Herpetomonas* in large numbers were found in the gut of sixteen insects.

ENTOMOLOGY.

The following biting flies caught in the Institute precincts represent comparatively rare insects at Yaba.

Ochlerotatus irritans 1 ♀.
O. domesticus 2 ♂.
Uranotænia cœruleocephala 1 ♂ 1 ♀.
U. balfouri 1 ♀.
Hodgesia cuptopous 2 ♀ ♀.
Culex insignis 5 ♂♂ 5 ♀ ♀.
C. thalassius 1 ♂.
Tabanus pluto 1 ♀.
Tæniorhynchus annetti 2 ♀ ♀.

Dr. K. K. Grieve collected at Ebute Metta.

Hodgesia sanguinis 2 ♀ ♀.
Ochlerotatus irritans 1 ♀.
O. nigricephalus 1 ♀.
Culex fatigans 1 ♂ 2 ♀ ♀.
~~*Culex fatigans* 1 ♂ 2 ♀ ♀.~~
C. decens 3 ♂♂.
Culiciomyia nebulosa 4 ♂♂ 6 ♀ ♀.
Mansonioides africana 1 ♀.

Dr. Hanington bred from larvæ at Bèan.
Culiciomyia nebulosa 13 ♀ ♀ 1 ♂.

Dr. Corson collected at Ibi.

Culex decens 6 ♂♂ 3 ♀♀.
C. fatigans 1 ♂ 6 ♀♀.
C. duttoni 24 ♂♂ 30 ♀♀.
C. tigripes 1 ♂ 2 ♀♀.
C. invidiosus 4 ♀♀.
Culiciomyia nebulosa 6 ♂♂.
Tæniorhynchus aurites 1 ♀.
Stegomyia luteocephala (bred from holes in Mango trees) 3 ♂.
S. (Aedes) fasciata (argenteus) 1 ♂.
Mansonioides africana 1 ♀.
Anopheles costalis 23 ♂♂ 8 ♀♀.
A. domicolus 1 ♀.
A. funestus 1 ♀.
Toxorhynchites phytophagus 1 ♀.
Hæmatopota pertinens 6 ♀♀.
H. bullatifrons 1 ♀.

Dr. Moiser collected at Kaduna.

Anopheles costalis 31 ♂♂ 140 ♀♀.
A. funestus 6 ♂♂ 64 ♀♀.
A. nili 3 ♂♂ 13 ♀♀.
A. mauritanus 5 ♀♀.
A. pharænsis 1 ♀.
A. domicolus 1 ♀.
Culex invidiosus 11 ♀♀.
C. decens 1 ♀.
C. duttoni 17 ♂♂ 9 ♀♀.
Culiciomyia nebulosa 19 ♂♂ 10 ♀♀.
Mansonioides africana 1 ♀.
Stegomyia (Aedes) fasciata (argenteus) 4 ♂♂ 4 ♀♀.

Dr. Stephens collected at Ilorin.

Tabanus tæniola 1 ♀.
Stomoxys calcitrans 5 ♀♀.
Glossina palpalis 4 ♀♀.
Ceratopogon castaneus 2 ♀♀.
Mansonioides africana 3 ♀♀.

Dr. Glover collected at Ikot-Ekpene.

Chrysops silacea 6 ♀♀.
C. dimidiata 1 ♀.

These were preserved in alcohol and were dissected on receipt. No larvæ of *Filaria loa* were found.

Dr. Sieger collected at Ossidinge.

Chrysops silacea 5 ♀♀.

These, also, were preserved in alcohol, and were found on dissection to contain no larvæ of *Filaria loa*.

The following experiments were done.

26/3/23. One female *Stegomyia (Aedes) fasciata (argenteus)* was not allowed a blood feed before it was put into a large bell jar along with two males of the same genus and species. A raisin was suspended from the top of the jar and a beaker of water was placed in the bottom of the jar. All three insects were reared from larvæ. One male died within four hours. Each day the female was offered a blood feed on a human arm, at 9 a.m. She consistently refused this until on the twelfth day of captivity she died, without having laid any eggs. On dissection, no sign of eggs could be seen. The second male predeceased the female by one day.

On the same day as the last experiment was begun, a similar one was done with two females and one male *Culiciomyia nebulosa*. All were bred from larvæ. The females refused a preliminary blood feed both on a guinea-pig and on a human arm. The jar in which the insects were confined contained banana as well as raisin, and a beaker of water. The females were daily offered a feed on a human arm. On the third day the male died and on the following day one female also succumbed. The remaining female survived for sixteen days, refusing the daily offer of a human arm. No eggs were laid, and none were seen in either female, on dissection.

Several experiments were performed as regards mating of males of *Culiciomyia nebulosa* with females of *Stegomyia* (*Aedes*) *fasciata* (*argenteus*), but these were invariably negative.

On two different occasions *Tæniorrhynchus annetti* ♀ was caught in the laboratory. The first was put into a glass jar containing a beaker in which floated some grass. Next day a raft of eggs was found on the water. The larvæ hatched out two days later.

Some ground rice was then put in the water, but apparently conditions were unfavourable as all the larvæ were dead by the third day.

The second *T. annetti* was put into a glass jar containing a beaker of water. Although bulging with eggs, no raft was laid, and after four days she was transferred to a test tube in which were water and some grass. This was kept in the dark and on the following morning a raft appeared. The larvæ hatched out in two days. These were transferred to a jar containing mud and pond water, but they were all dead at the end of twenty-four hours.

On 1st October twenty *Mansonioides africana* ♀ obtained from neighbouring native houses were released into a large bell jar, containing a beaker of water on which floated grass and water weeds. On 5th October two rafts of eggs were found floating on the water. The larvæ hatched out on 9th October but all were dead three days later.

On 15th October six *M. africana* ♀ collected by labourers from their houses were put into a jar containing a beaker of water on which floated water weeds and grass. Three days later a cluster of eggs was laid on a leaf close to the water. The larvæ hatched out in three days but survived only two days.

The following dissections were done, under the binocular microscope.

Mosquitoes collected by Sanitary Inspectors in Lagos.

Anopheles costalis 2 ♀ ♀ negative.

Stegomyia (*Aedes*) *fasciata* (*argenteus*) 4 ♀ ♀ negative.

Culiciomyia nebulosa 1 ♀ negative.

Culex fatigans 5 ♀ ♀ negative.

Three *Mansonioides africana* were induced to feed on a native who showed a few subtertian rings in his blood. One died three days afterwards and the remaining two were killed on the seventh day. No oocysts were found in the stomach nor were sporozoites observed in the salivary glands.

A collection of *Tabanus* preserved in 80% alcohol was received from Dr. Corson at Ibi. The individuals were

<i>T. taeniola</i>	15
<i>T. secedens</i>	10
<i>T. fasciatus</i>	1

There was also one specimen of *Glossins tachinoides*. A search was made in all for the larvæ of *Filaria*, but the result was uniformly negative.

As noted elsewhere in this report, many bugs and lice were dissected in a search for the spironema of relapsing fever, and also a number of *Mansonioides africana* after having fed on a patient in whose blood there were embryos of *Acanthocheilonema perstans*.

Most of the year however, has been taken up with the systematic dissection of mosquitoes brought in by the labourers from the native houses in the vicinity of Yaba. Every Saturday evening each labourer was provided with several plugged test tubes and told to collect mosquitoes from his house, particularly those which had bitten him. This lessened the likelihood of his filling the test tube with male specimens. A bribe was offered for the largest collection each Monday morning.

As it was quite impossible, on account of the presence of blood in the stomach to dissect the whole collection in one day, the weaker specimens were worked on first and the others fed on sugar-water.

It was somewhat of a surprise to find that *Mansonioides africana* greatly outnumbered all the other mosquitoes brought in. The actual number was 4,027 of which 3,064 were dissected, the others having died before their blood feed was digested.

Larvæ of *Filaria* were found in the proboscis of one, and in the muscles of the head and thorax of another.

Small nematodes were found in the stomach of two, and in a third, two much larger nematodes were noted, one extending from the thorax into the abdomen and the other coiled at the tip of the abdomen.

Spironemata were observed in the stomach of five individuals but their numbers were small. On one occasion the stomach contents, in a little saline were injected into the peritoneum of a rat, but the inoculation was unproductive.

Amœbæ and other protozoa were occasionally found in the stomach, most probably derived from the water in which the insect hatched, but none was of known pathogenic importance. *Herpetomonas* were noted in the stomach contents on one occasion.

In ten specimens however there were structures resembling developmental forms of *Proteosoma* or *Plasmodium*. There were bodies resembling oocysts in the stomach wall of seven, and structures similar to sporozoites in the salivary glands of four, one insect showing both types of structures.

298 *Anopheles costalis* were collected of which 198 were dissected; of these, forty were found to be infected with malaria, and twelve with filaria. Eleven showed sporozoites in the glands but nothing in the stomach. Twenty-one showed oocysts in the stomach but nothing in the glands. Eight had the parasite both in the glands and in the stomach.

Three of the insects with the stomach only infected contained also filaria and two mosquitoes with a malarial infection of both stomach and glands showed also very numerous filariae in the head and thorax.

The other mosquitoes dissected were:—

Culiciomyia nebulosa, fourteen, all negative.

Culex rima, eight, one with *Herpetomonas* in stomach, seven, negative.

C. fatigans, five, one with filaria, four negative.

C. thalassius, five, one with? oocysts on stomach wall, four negative.

Ochlerotatus irritans, five, all negative.

Stegomyia (Aedes) fasciata (argenteus) four, all negative.

Culex tigripes, two, negative.

C. quasigelidus, two, negative.

C. grahami, one, negative.

C. duttoni, one, „

Anopheles umbrosus, one, negative.

Taeniorrhynchus annetti, one, negative.

The differences between the stomachs of the various mosquitoes and also between their glands, are remarkable. The stomach of *Mansonioides africana* is very tough, as are also the glands which usually have bifurcations at the tips. The glands and the stomach of *Culiciomyia nebulosa* are extremely soft and very easily burst.

A record was kept for six months, of the number of rafts of mosquito eggs laid in a barrel which received the waste water from a wash-hand basin. The rafts were counted each morning, after which they were removed singly, and the barrel emptied. No note was made of single eggs laid.

The figures are :—

January	339 rafts.
February	302 „
March	186 „
April	295 „
May	354 „
June	1,134 „

The month of March may be regarded as the end of the dry season. Most of the rafts were laid by *Culex decens* and by *Culiciomyia nebulosa*.

MOSQUITO LARVÆ.

As in the past, collections of mosquito-larvæ made by the Sanitary Inspectors on their daily rounds in the Municipal area of Lagos were kindly sent by the Medical Officer of Health, Dr. R. W. Orpen, to the Institute for identification. 868 collections were received and in Table VI will be found the receptacle and the larvæ as identified. It will be seen that, as formerly, the larvæ of *Aedes (Stegomyia) argenteus (fasciata)* greatly outnumber the others, the total collections being 634, and the favourite breeding place being the house-hold water pots and other receptacles containing, in most cases clear water. *Culiciomyia nebulosa* is next in order of frequency, occurring as it did in 216 receptacles. The favourite breeding medium for this mosquito is a liquid containing much decomposing and malodorous matter such as "agbo" and native dyes. The other mosquitoes hatching out from the collections were *Culex fatigans* eighteen, *Anopheles costalis* twelve, *Culex decens* eight, *Ochlerotatus irritans* seven, *Stegomyia luteocephala* two, *Culex tigripes* two, and *Culex insignis* one.

CLINICAL MATERIAL.

During the year 434 samples of fæces have been examined at the Institute. The colour, the consistence and the presence or absence of mucus are noted in the ledger. In the accompanying Table No. VII, the samples have been divided into six groups, according as they were formed, pultaceous or liquid and with or without mucus. It will be noted that nearly half of the total fall into the third group, that is pultaceous in appearance and without mucus. The number placed under "liquid" without mucus, is the next largest, and "formed" fæces form the smallest double group. This is in accordance with the general belief, that in the tropics, formed fæces are the exception not the rule.

The liquid fæces, providing the next largest group is an indication of the liability to gastro-intestinal disorders in the tropics.

The percentage of negative findings in the formed and in the pultaceous group is very similar, i.e. 41% in the first and 44% in the latter. In the liquid group, the percentage is not quite so high, being just over 38 but in this case the comparatively high figure is an indication of the prevalence of gastro-intestinal irritation due to diet or some cause other than protozoal.

The percentage of negative findings however falls very low, in the groups in which mucus is present. Associated with this, the proportion of findings of *E. histolytica* and of pus and epithelial cells is very greatly higher than in the groups where mucus is not noted.

Other facts worthy of notice are, the large number of cases in which *Blastocystis* was found, and also the prevalence of *Trichocephalus* and *Ascaris*. The last two are mainly found in the stools from natives, of which there were 116 samples.

Entamoebae histolytica occurred in forty Europeans and thirty-two natives.

Lamblia was met with in thirteen Europeans and three natives.

It should be added that spirochætes were noticed in most samples of fæces but they were particularly abundant in the case with liquid fæces included in the table.

TABLE VII.

	Formed	Formed with mucus.	Pulta- ceous.	Pulta- ceous with mucus.	Liquid.	Liquid with mucus.
Total	34	27	212	31	88	42
Negative	14	2	94	3	34	1
<i>E. histolytica</i>	*5	†8	‡13	\$11	10	†25
Epithelial and pus cells ...	2	24	20	26	14	41
Red blood cells	1	...	1	...	14
Charcot Leyden Crystals ...	1	2	3	...	2	...
<i>E. coli</i>	3	1	15	...	3	...
<i>E. nana</i>	2	1	9	...	5	...
<i>I. bütschlii</i>	1	...	8	...	3	...
<i>Lamblia</i>	1	...	10	1	3	1
<i>Tetramitus</i>	6	...	6	1
<i>Trichomonas</i>	3
<i>Embadomonas</i>	1	...
<i>Ceetomonas</i>	1	...	2	...
<i>Spirochaetes</i>	1	...
<i>Blastocystis</i>	7	1	37	...	20	...
<i>Trichocephalus</i>	9	2	35	...	11	1
<i>Ascaris</i>	6	2	34	5	11	1
<i>Ankylostome</i>	1	1	18	4	9	1
<i>Strongyloides</i>	2	...	5	...	1	...

*All in cyst-stage. †All in active stage. ‡Cysts only in 8. \$All active amoebae. ||Only four in cyst-stage.

BLOOD SMEARS.

Blood smears form the next largest series of specimens examined, 299 from Europeans and 107 from Natives a total of 406. Subtertian malarial parasites were found in forty-one, thirty Europeans and eleven Natives. Crescents were noted on three occasions, on two of which they were ^{the} only stage of the parasite seen. The quartan parasite, in the ring form and in the ~~gametocyte~~ ^{gametocyte} stage was met with in only one patient, a native. The benign tertian parasite was not encountered. Pigmented mononucle~~ar~~ or leucocytes were seen on three occasions in the absence of malaria parasites.

The embryos of *Filaria loa* were observed in the blood of eight persons, five Europeans and three Natives.

Forty-nine differential leucocyte counts were made and the Arneeth formula was ascertained in thirty-one instances.

URINE.

Ten specimens were examined. Red blood cells and pus were found in three, and pus in two.

SPUTUM.

Thirty-eight samples were stained for the tubercle bacillus. The findings were positive in nine (European three, Native six).

WIDAL TEST.

Serum from six patients reacted positively to bacillus paratyphosus B in three instances and the result was negative in the remainder.

VACCINES.

Sixteen vaccines were prepared.

MISCELLANEOUS.

Smears. Twenty smears were received, seven taken from skin eruptions, four of pus from the eye, three of gland juice, three from the nose, and one each from cerebro-spinal fluid, an ulcer of the lip and an ulcerated tonsil.

Fluid. Two samples of pleural exudate and one from a knee joint were examined.

Water Analysis. Six samples of water were submitted to a bacteriological analysis.

HISTO-PATHOLOGY.

The following organs were sectioned and reported on, Liver, five specimens, Spleen five, Brain five, Lung three, and Kidney two specimens.

Sixteen specimens of Carcinoma were received. Epithelioma of toe two, of foot, of leg, of scrotum, of penis, of buttock, and of lip. Carcinoma of rectum two, of breast two, of bladder, of stomach, of face and of testis.

Sarcomas numbered thirteen, of jaws three, of foot three, of testis two, of chest, of abdominal wall, of femur of thigh and of scrotum.

The following simple tumours occurred.

Cutaneous horn, Lipoma, Fibro-myxo-adenoma of Parotid, ~~C~~érsoid Aneurysm, Epulis, Fibroma of scalp, Fibroma of lip. Adenoma of breast and Polypus from nares.

Other specimens were Gumma of muscle, Gumma of gland, Tubercular disease of gland, Elephantiasis of scrotum, Chronic inflammatory conditions, cervix uteri, scrotum, thumb, heel, shoulder and psoas muscle. Three pieces of skin were examined for leprosy, two tumours were found to be occasioned by *Onchocerca volvulus* and ~~t~~ubercular disease was found in one specimen of Fallopéan tube.

VENEREAL.

During the year the Sachs Georgi test was applied to fifty-three samples of serum. The result was positive in nineteen.

Sixteen smears from chancres were examined and *Spironema pallidum* was demonstrated in three. Pus obtained by prostatic massage in four cases showed the gonococcus in all. Three smears from the discharge from the penis, showed this organism in two. A vaginal smear was negative.

The following sent specimens to the Institute. Dr. Adam, Dr. Adcock, Dr. Aitken, Dr. Birt, Dr. Booth, Dr. Braithwaite, Dr. Cauchi, Dr. Corson, Dr. Craig, Dr. Cummings, Dr. Digby, Dr. Dyce-Sharp, Dr. Fetherston-Dilke, Dr. Gallagher, Dr. Glover, Dr. Gray, Dr. Grey, Dr. Grieve, Dr. Hanington, Dr. Kelsall, Dr. Leonard, D.S.O., Dr. Mackey, Dr. McLeay, Dr. Maples, Dr. Martyn-Clark, Dr. Moiser, Dr. J. J. Moore, Dr. Fitzgerald Moore, Dr. Morehead, Dr. Neal, Dr. Nicholson, Dr. O'Keeffe, Dr. Orpen, Dr. Parkinson, Dr. Pollard, Dr. Ross, Dr. C. J. Sharp, M.C., Dr. Sieger, Dr. Stephens, Dr. Stirrett, Dr. Thomson, Dr. Waldron, Dr. Walker, Dr. A. H. Wilson, and Dr. G. Wilson.

THE CLINICAL LABORATORY.

The Clinical Laboratory at Lagos fulfilled its function, although unfortunately it was not possible to have a medical officer in charge, for a large part of the year. Consequently, from a lack of continuity, a detailed report is not available and only bare figures can be given. A study of these will show that a large amount of work has been done.

The total number of blood smears examined was 572 of which 435 came from Africans and 137 from Europeans. The cases in which subtertian malarial parasites were observed numbered thirty-seven in each group, a total of seventy-four. The only other parasites noted are *spironema* in five cases, and these have been more fully described elsewhere in this report.

Fifty-three differential leucocyte counts were made, nine total red and white cell counts, and eight hæmoglobin estimations.

As regards fæces, 385 samples were examined, 334 from Africans and fifty-one from Europeans.

The findings in the latter were *E. histolytica* in two, other protozoa in three, *Ascaris* ova in three and *Trichocephalus* ova in one. Amongst the natives *E. histolytica* was present in twelve, other protozoa in seventeen, *Ascaris* ova in 143, *Trichocephalus* ova in eighty-three, *Ankylostome* ova in fifty-seven, *Schistosoma* ova in three, *Strongyloides* ova or larvæ in twenty-two and ova of *T. saginata* in two.

Ninety specimens of sputum were examined for tubercle bacilli. The findings were negative in Europeans but were positive in twenty-one of seventy-eight Natives.

203 examinations of urine were made. Schistosome ova were found in three out of 177 Natives.

Forty-five smears from various sources were examined. The gonococcus was demonstrated in nine, and a spirochæta in two. A smear from an abscess in the leg of a native showed enormous numbers of spirochætes many of them occurring in felted masses.

The Sachs Georgi reaction was performed in 109 cases with a positive result in forty-eight.

Two Widal agglutination tests were made.

Tissues examined histologically numbered ninety-six.

113 post-mortem examinations were carried out, either in the hospital or in the public mortuary.

Dr. Q. Stewart, whilst he was in charge of the laboratory at the beginning of the year, made a very useful collection of post-mortem specimens all beautifully preserved and mounted.

Dr. Clive Sharp, M.C., during the last few weeks of the year, carried out an extensive search for "microfilaria~~e~~" in the skin, already described in this report. He also made a routine examination in all cases post-mortem, for coccidial infection of the gut.

A. CONNAL,

Director, Medical Research Institute.

